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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,503	09/25/2003	Shigeru Kawano	21581-00256-US1	4338

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EXAMINER	
PAK, YONG D	
ART UNIT	PAPER NUMBER
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/21/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

T6

Office Action Summary	Application No.	Applicant(s)	
	10/669,503	KAWANO ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16-18 and 33-37* is/are pending in the application.

4a) Of the above claim(s) *1-11,18 and 33-37* is/are withdrawn from consideration.

5)☒ Claim(s) *14* is/are allowed.

6)☒ Claim(s) *12,13,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 September 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/787,746.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a divisional of 09/787,746, now abandoned.

The amendment filed on October 12, 2006, amending claims 1-2, 6-14, 16-17 and 33-35 and canceling claim 15, has been entered.

Claims 1-14, 16-18 and 33-37 are pending. Claims 1-11, 18 and 33-37 are with drawn. Claims 12-14 and 16-17 are under consideration.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on October 12, 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Response to Arguments

Applicant's amendment and arguments filed on October 12, 2006, have been fully considered and are deemed to be persuasive to overcome some of the objections/rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Biological Deposit

The Declaration filed on October 12, 2006 satisfies the biological deposit requirements of the *Candida maris* IFO 10003.

Sequence Compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that the nucleic acid sequence in Figure 1 lacks sequence identification numbers. See particularly 37 CFR 1.821(d). Figure 1 has been amended to recite "SEQ ID NO:1" for the amino acid sequence, but lacks a sequence identification number for the nucleic acid sequence.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-13 and 16-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 12-13 and 16-17 are drawn to a reductase isolated from any or all *Candid or Candida maris* source or from *Candida maris* IFO 10003, including any or all mutants, variants and recombinants thereof, and having the properties and characteristics recited in the claims 12 and/or 13. Therefore, the claims are drawn to a genus of polypeptides having any structure. The specification only teaches one

species, the reductase comprising the amino acid sequence of SEQ ID NO:1 isolated from *Candida maris* IFO 10003 and having the recited properties. One species is not enough and does not constitute a representative number of species to describe the whole genus and there is no evidence on the record of the relationship between the structure of the reductase of SEQ ID NO:1 and the structure of any recombinants, variants and mutants of any reductase isolated from any or all *Candida or Candida maris* source or from *Candida maris* IFO 10003, including variants, mutants and recombinants thereof. Therefore, the specification fails to describe a representative species of the genus comprising reductase derived from "*Candida*", "*Candida maris*" or "*Candida maris* IFO 10003", including any or all variants, mutants and recombinants thereof.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 12-13 and 16-17.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that since claims 12 and 13 have been amended to recite the origin of the enzyme, persons skilled in the art could obtain the enzymes of the claims. Examiner respectfully disagrees. Claims 12-13 and 16-17 are drawn to a reductase islated from any or all *Candid or Candida maris* source or from*Candida maris* IFO 10003, including any or all mutants, variants and recombinants thereof, and having the properties and characteristics recited in the claims 12 and/or 13. Therefore, the claims are drawn to a genus of polypeptides having any structure. In *University of Calfornia v. Eli Lilly & Co.,* 43 USPQZd 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, (or) chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

The recitation of the physical and chemical properties recited in claims 12 and 13 fail to provide a sufficient description of the claimed genus of proteins as it merely describes the functional features of the genus without providing any definition of the structural features of the species within the genus. The CAFC in UC California v. Eli Lilly, (43 USPQ2d 1398) stated that: "in claims to genetic material, however a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." Similarly with the claimed genus of reductase proteins, the functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the protein species within the genus from other proteins such that one can visualize or recognize the identity of the members of the genus. Further, while MPEP 2163 acknowledges that in certain situations "one species adequately supports a genus," it also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." In view of the widely variant species encompassed by the genus, this one example is not enough and does not constitute a representative number of species to describe the whole genus of any or all polypeptides

having the recited activity isolated from any or all *Candid or Candida maris* sources or from *Candida maris* IFO 10003, including any or all variants, recombinants and mutants thereof, and there is no evidence on the record of the relationship between the structure of the reductase of SEQ ID NO:1 and the structure of any or all recombinant, variant and mutant of any or all reductases isolated from any or all *Candid or Candida maris* sources or *Candida maris* IFO 10003.

Hence the rejection is maintained.

Claims 12-13 and 16-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the reductase comprising the amino acid sequence of SEQ ID NO:1, does not reasonably provide enablement for (A) any reductase isolated from any or all isolated from *Candida or Candida maris* source or *Candida maris* IFO 10003, including recombinants, variants and mutants thereof, and having the recited properties. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 12-13 and 16-17 are drawn to a reductase isolated from any or all *Candid or Candida maris* source or from *Candida maris* IFO 10003, including any or all mutants, variants and recombinants thereof, and having the properties and characteristics recited in the claims 12 and/or 13. The claims encompasses any reductase isolated from any or all *Candida or Candida maris* source or from *Candida maris* IFO 10003, including recombinants, variants and mutants thereof, and having the recited properties. Therefore, the claims are drawn to a genus of polypeptides having any structure. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a reductase isolated from *Candida maris* IFO 10003 having the amino acid sequence of SEQ ID NO:1. It would require undue experimentation of the skilled artisan to make and use the claimed variants, mutants and recombinants of SEQ ID NO:1 or a reductase isolated from any *Candida or*

Candida maris source or from *Candida maris* IFO 10003, including any or all mutants, recombinants or variants thereof. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass encompasses any reductase isolated from any or all *Candida or Candida maris* source or from *Candida maris* IFO 10003, including recombinants, variants and mutants thereof, and having the recited properties, because the specification does not establish: (A) regions of the protein structure which may be modified without affecting its enzymatic activity; (B) the general tolerance of a reductase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid

residue with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including variants, mutants and recombinants of SEQ ID NO:1 or a reductase isolated from any *Candida or Candida maris* source or from *Candida maris* IFO 10003, including any or all mutants, recombinants or variants thereof. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of variants, mutants and recombinants of SEQ ID NO:1 or a reductase isolated from any *Candida or Candida maris* source or from *Candida maris* IFO 10003, including any or all mutants, recombinants or variants thereof having the desired biological characteristics recited in the claim is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that since claims 12 and 13 have been amended to recite the origin of the enzyme, persons skilled in the art could obtain the enzymes of the claims without undue experimentation. Examiner respectfully disagrees. Claims 12-13 and

16-17 are drawn to a reductase derived from any or all *Candid or Candida maris* source or *Candida maris* IFO 10003, including any or all mutants, variants and recombinants thereof. As discussed above, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a specific knowledge of and guidance with regard to which specific amino acids in the protein's sequence, can be modified such that the modified polypeptide continues to have said claimed activity. It is this specific guidance that applicants do not provide. Without specific guidance, those skilled in the art will be subjected to undue experimentation of making and testing each of the enormously large number of mutants that results from such experimentation. While the art may teach in general the structure of the reductase having the amino acid sequence of SEQ ID NO:1 isolated from *Candida maris* IFO 10003, conserved amino acid sequences, and etc, such teachings will not reduce the burden of undue experimentation on those of ordinary skill in the art.

Hence the rejection is maintained.

Allowable Subject Matter

Claim 14 is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

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